STEREOSPECIFIC OLEFIN SYNTHESIS <u>VIA</u> BORONIC ESTERS. STUDIES RELATED TO PROSTAGLANDIN SYNTHESIS

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The utility of organoboranes in stereospecific olefin synthesis is now well recognized.² Of particular interest to us for synthetic studies currently in progress has been the boronmediated cross-coupling reactions shown below (Scheme I) which result in the stereospecific

Scheme I



synthesis of either <u>E</u> or <u>Z</u>-1,2-disubstituted olefins.³ Although the decomposition of vinylborane 1 with the indicated reagents affords olefins 2 and 3 with <u>ca</u> 95% stereospecificity, the overall reaction sequence is flawed by the fact that only one of the carbon ligands attached to boron is utilized in the cross-coupling process. One solution to this general problem has been to employ "mixed" dialkylboranes where one of the boron-bound carbon ligands (e.g., thexyl) demonstrates a low migratory aptitude.⁴ However, it is now becoming clear that the definition of a hierachy of migratory aptitudes is both reaction specific and substrate dependent.⁵ A case in point is the observation that thexyl and alkenyl ligands show comparable migratory capabilities in the vinylborane iodination process $1 \rightarrow 2$.^{5a} This present study (<u>vide infra</u>) provides further support to the preceding contention.

In conjunction with our interest in developing efficient stereospecific olefination reactions for projected prostaglandin syntheses, we have investigated the boron-mediated crosscoupling process outlined in Scheme II. Since oxygen ligands do not compete with carbon in the rearrangements of boron <u>att</u>-complexes,⁶ we were interested in ascertaining whether intermediates 6 and 9 could be induced to couple to give the Z and E-olefins 7 and 10 respectively.⁷ Accordingly, boronic ester 4 (bp, 40°/1 mm) was prepared in direct analogy to the procedure reported by Brown,⁸ while the E and Z-vinyllithium reagents 5 and 8 were prepared from the corresponding vinyl iodide.^{9,10} <u>via</u> metal-halogen exchange (<u>s</u>-butyllithium, -78°).

Scheme II



Addition of boronic ϵ ster 4 (1 equiv) to a solution of 5 (1 equiv) in tetrahydrofuran (THF) at -45° followed by the addition of nodine (1 equiv) and subsequent stirring at 25° (3 hr) afforded the desired <u>Z</u>-olefin <u>7a</u> (22%) as well as vinyl iodide <u>lla</u> (22%) and olefin <u>llb</u> (11%). Control



experiments established that vinyl iodide 11a was derived from competing reaction of the atecomplex 6 and not free vinyllithium reagent 5. Attempts to improve the yield of 7A by the use of a large excess of iodine and by the addition of bases resulted in minor changes in the 7a:lla ratio but little change in the absolute yield of the desired Z-olefin. Similar observations were made in attempted rearrangement of ate-complex 9. After a careful study of the iodinepromoted rearrangement of both 6 and 9, we have found that the yield of olefin can be improved dramatically by carrying out the rearrangement of 6 in methanol-THF (2:1) in the presence of sodium methoxide. Under these modified conditions boronic ester 4 can be condensed with vinyllithium reagents 5 and 8 and rearranged to the respective olefins 7a (75%) and 10a (58%). 11 Typical experimental procedures follow: To a cooled (-78°), THF solution (6 ml) of E-iodide 11a⁹ (1 mmol) was added 2 mmol of s-butyllithium (0.7 M, hexane). After 1 hr the temperature was raised to 0° and boronic ester 4 (1 mmol) was added. After 10 min, ate-complex 6 was decomposed by the consecutive addition of 3 equiv of sodium methoxide-methanol (1 ml) followed by iodine (5 equiv) in 10 ml of methanol. Extractive workup afforded the Z-olefin 7a in 75% yield.^{11,12} Similar experimental procedures employing vinyllithium reagent <u>8</u>¹⁰ prepared in ether afforded the E-olefin 10a in 58% yield. 11,12

To determine the <u>E:Z</u>-isomer ratio from each cross-coupling reaction, allylic alcohols *7b* and <u>10b</u> were prepared. ^{11,13} The conversion of *7a* to *7b* was carried out in \geq 90% yield (Bu₄NF, THF), while the transformation of <u>10a</u> to <u>10b</u> was accomplished under standard conditions (HOAC; H₂0, 55[°]). Gas chromatographic analysis revealed that the conversion of 4 to <u>7b</u> was approximately 95% stereospecific while the transformation of 4 to <u>10b</u> was effected with \geq 99% stereospecificity.

A comparison of the boronic ester-mediated olefin synthesis to the Zweifel olefination process³ (Scheme I) is instructive. Monohydroboration of the illustrated acetylene with bis-2-ethylcyclopentylborane (12a) followed by basic iodine decomposition³ afforded the Z-olefin Za in 36% yield (based on 1-ethylcyclopentene). In an attempt to improve the efficiency of olefin-acetylene cross coupling the analogous reaction was carried out with the mixed borane 12b containing thexyl (C_6H_{13}) and 2-ethylcyclopentyl (C_7H_{13}) ligands. In this instance a 30% yield of Za and 14% of 13 were obtained. As anticipated from earlier work, significant thexyl ligand migration was observed. These results are to be compared with the modified



olefination sequence (Scheme II) which afforded $\underline{7a}$ in 75% yield. Furthermore, attempts to obtain the <u>E</u>-olefin <u>10c</u> via acetylene monohydroboration with either <u>12a</u> or <u>12b</u> followed by cyanohalogenation^{3b} (<u>c.f.</u> <u>1</u> \rightarrow <u>3</u>) failed to yield any of the desired product. The major olefinic material obtained in this reaction showed nitrile incorporation and loss of silyl ether

To date, the use of boronic esters in carbon-carbon bond constructions has been quite limited.^{6,7} However, these organofunctional species offer a general solution to some of the problems of stoichiometry in the organoborane area of organic synthesis. Applications of this versatile olefin synthesis will be reported in due course.

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- 12. Yields determined by glc using internal standards.
- 13. Both 7a and 10a were obtained as a mixture of alcohol-protected diastereoisomers.